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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/713,177	11/15/2000	Glen H. Erikson	E1047/20048	3217

3000 7590 06/05/2002

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EXAMINER

CHUNDURU, SURYAPRABHA

ART UNIT PAPER NUMBER

1637

DATE MAILED: 06/05/2002

14

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/713,177

Applicant(s)

ERIKSON ET AL.

Examiner

Suryaprabha Chunduru

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 22 May 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-63 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-63 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

**Supplemental Action**

1. The previous office action (mailed on 4/26/2002) has been withdrawn in view of the request for reconsideration of IDS. The pending claims 1-63 in this instant application are considered for examination in this office action.
2. The Information Disclosure Statement (paper No.12) filed on April 12, 2002 and April 24, 2002 have been entered and considered.
3. The Information Disclosure Statement (Paper No. 10 and 12) filed on April 11, 2002 and April 29, 2002 has been entered.

**Response to Arguments**

4. Applicant's response to the office action (Paper No.8) is fully considered and is found persuasive in part.
5. With respect to the rejection made in the previous office action under 35 U.S.C. 103(a), applicants amendment and arguments have been considered the rejection is withdrawn herein.

**New Grounds of Rejection necessitated by Amendment**

***Claim Rejections - 35 USC § 112***

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-63 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the

Art Unit: 1637

art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

“ factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims”.

#### The nature of the invention

Claims 1-23 and 62-63 are drawn to a catalytic hybridization composition comprising a multiplex structure involving Watson-Crick base pairing with more than two strands and with dependent claims further limiting conditions in the formation of multiplex structure. Claims 24-61 are drawn to a method of hybridization assay comprising formation of the said multiplex structure. The invention is a class of invention, which the CAFC has characterized as “the unpredictable arts such as chemistry and biology.” *Mycogen Plant Sci., Inc. v. Monsanto Co.*, 243 F.3d 1316, 1330 (Fed.Cir.2001).

The Breadth of the claims

The claims encompass a catalytic hybridization composition comprising a multiplex structure involving Watson-Crick base pairing with more than two strands and a method of hybridization assay for formation of the said structure. The specification does not provide any structure formation of multiplex with the specific Watson-Crick base pairing among the nucleic acid strands.

Quantity of Experimentation

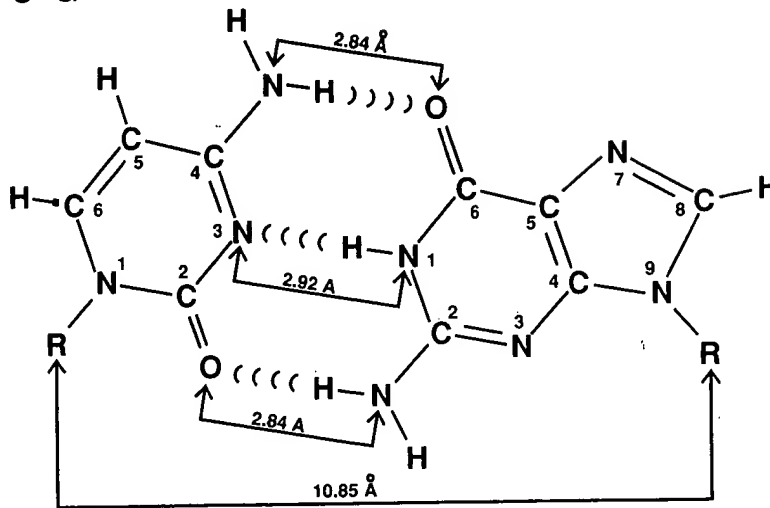
The quantity of experimentation in this area is extremely large since structural identity of the multiplex structure of nucleic acid would initially require, in vitro studies to demonstrate proof of principle. That is, prior to any structural intervention, it would be necessary to create a crystallographic or NMR (nuclear magnetic resonance) structure, show that the structure occurs in sufficient stability and then show stability of the structure is associated with Watson-Crick base pairing with more than two strands, a series of showings not present in the specification. Following such experimentation, the multiplex structure of nucleic acids would need to be characterized and stability of the structure would need to be demonstrated. This would require years of inventive effort, with each of the many intervening steps, upon effective reduction of practice, not providing any guarantee of success in the succeeding steps.

The unpredictability of the art and state of art

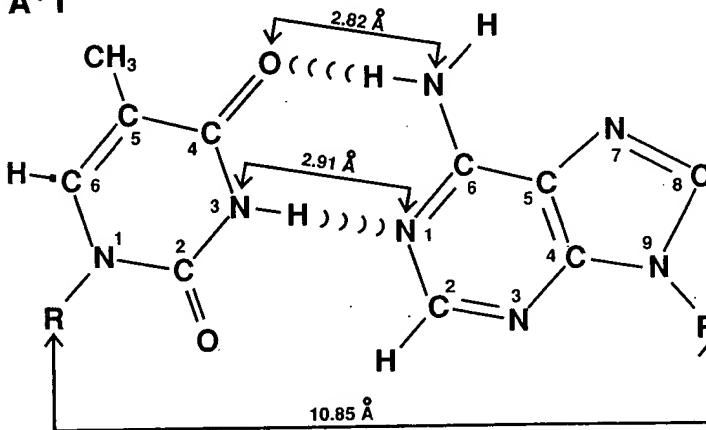
Predictability in the art suggests interaction of two strands in a duplex involves Watson-Crick bonding. Hydrogen bonding and base stacking hold a duplex DNA helix together as shown in the following Fig. 1.7.

Art Unit: 1637

C•G



A•T



**Figure 1.7 Watson-Crick base pairs.** The interatom hydrogen bond distances and distances between the C1' positions of the ribose sugars are indicated. The curved lines represent the hydrogen bonds. The curves are in the direction of the hydrogen bond acceptor (N or O atoms). Figure modified with permission from Arnott *et al.* (1965).

As shown in the Fig 1.7, a hydrogen bond is a directional interaction between a covalently bound H atom and a nitrogen or oxygen of a base (adenine (A), thymine (T), Guanine (G), cytosine (C)). In the C.G base pairing it is apparent from the figure that the middle N-H hydrogen bond would be inaccessible for any other strand for Watson-crick pairing. A reverse Watson-crick base pairing occurs when one nucleotide rotates  $180^\circ$  with respect to complementary nucleotide. This type of base pairing is found in Hoogsteen base pairing. The

Art Unit: 1637

instant specification does not provide any pictorial or space-filling model to show the Watson-Crick pairing in the multiplex structure.

Further, it is also evident from the prior art that Watson-Crick double helix structure of DNA (B-form) is right handed and the common form, originally deduced from X-ray diffraction analysis. As shown in the Fig. 1.14 A and B below, a dominant feature of B-form DNA is the presence of major and minor grooves. Different functional groups on the purine and pyrimidine base are accessible from major or minor grooves. The Watson-Crick hydrogen bonding surfaces are not available to solvents or proteins, since functional groups involved in hydrogen bonding are interacting with each other at the center of the double helix. The Hoogsteen bonding surface of purine is accessible through major groove. It is apparent from the figure that the Watson-Crick hydrogen bonding surfaces are inaccessible for any other strands since two strands are already interacting with each other at the center of the double helix.

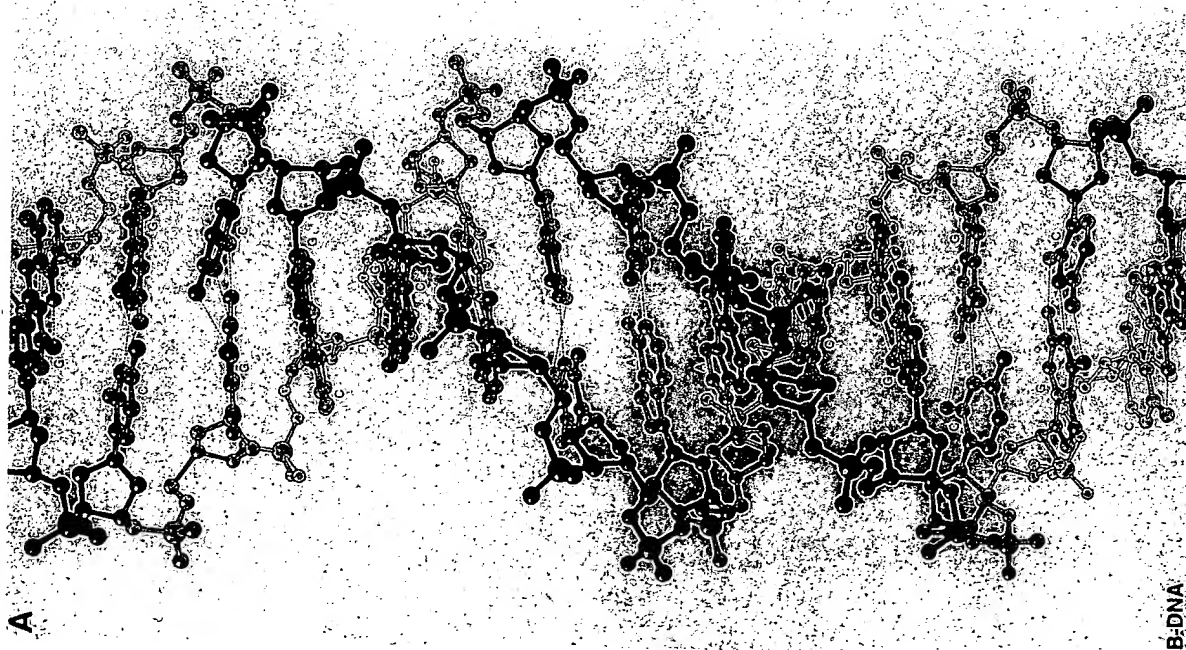
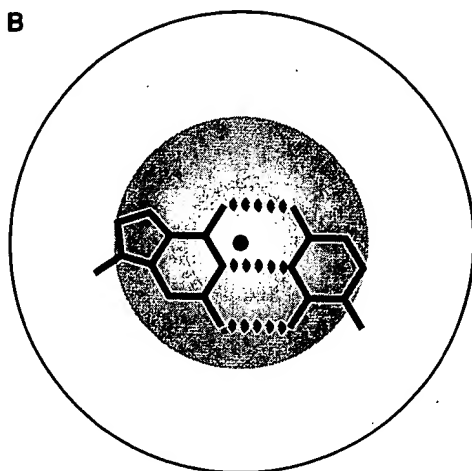


Figure 1.14 B-DNA helix. (A) In this model of the B-DNA helix the phosphate backbones can be seen as smooth right-handed coils on the outside of the helix. This view looks into a minor groove at the center of the model. Major grooves are seen above and below the minor groove. (Copyright by Irving Geis.)



**Figure 1.14** *Continued.* (B) In the B-DNA helix the hydrogen bonded base pairs are stacked near the center of the helix. The center of the helix passes nearly symmetrically through the Watson-Crick hydrogen bonds.

The prior art also indicates that the triple helix does not represent the most thermodynamically stable structure that can be adopted by two complementary poly purine. poly pyrimidine strands. There is a loss of Watson-Crick hydrogen bonding in a triplex DNA formation (see page 225, Fig 6.4 and paragraph 1).

The instant specification, would not be easily translatable to (i) the multiplex structure formation with a single hydrogen bond interacting with more than two strands utilizing Watson-Crick base pairing; (ii) crystallographic or NMR predicted model for the multiplex structure of the claimed invention. The unpredictability of multiplex structure is evidenced by the prior art,



Art Unit: 1637

which fails to support Watson-Crick base pairing in triplex formation and in fact support unpredictability of this area of technology.

#### Working Examples

The specification failed to show any working examples regarding physical structure based on crystallography or NMR model or X-ray diffraction analysis for multiplex structure. The Exhibit C in the specification show the fluorescent intensity as a function of binding affinity between target and probe strands, but do not provide any evidence for the physical structure for the multiplex structure with Watson-crick base pairing among the multiple strands of nucleic acids.

#### Guidance in the specification

The specification, while providing a general review of various nucleic acid structures, does not provide teachings sufficient to overcome doubts raised in the art with regards to the stability of multiplex structure. No specific teachings regarding the use of multiplex structure in assaying triplex and quadruplex nucleic acid complexes. It would be essentially be a trail and error process, to make and use of the diverse species of multiplex structure of nucleic acids encompassed by the claims. No space filling model or structural model of the interaction involving Watson-Crick base pairing with more than two strands is provided.

#### Level of skill in the art

The level of skill in the art is deemed to be high.

#### Conclusion

In the instant case, as discussed above, the level of unpredictability is high, the specification provides no written description or guidance that leads one to a reliable or stable

Art Unit: 1637

multiplex structure. One skilled in the art cannot readily anticipate the effect of change within the subject matter to which the claimed invention pertains. Further the specification does not provide guidance to overcome art recognized problems in multiplex structure formation. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance and direction provided in the specification, the absence of any working examples and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claimed invention as broadly written.

***Claim Rejections - 35 USC § 101***

7. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1- 63 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

The current claims are drawn to a catalytic hybridization composition and a method comprising multiplex structure with more than two strands of nucleic acid interacting with Watson-Crick base pairing.

Following the requirements of the Utility Guidelines (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for Utility.), the first inquiry is whether a credible utility is cited in the specification for use of the multiplex structure. Some of the cited utilities identified by the examiner are to detect the nucleic acid itself and to use as a probe. These utilities are credible. However, the basic multiplex structure involving Watson-Crick base

pairing with more than two strands is incredible and use of such structure is incredible based on unpredictability of the multiplex structure involving Watson-Crick pairing with more than two strands, as discussed above in the enablement rejection under U.S.C. 112, first paragraph.

Further, MPEP 2107.02 states that “In many of these cases, the utility asserted by the applicant was thought to be “the Office considered the asserted utility to be inconsistent with known scientific principles or “speculative at best” as to whether attributes of the invention necessary to impart the asserted utility were actually present in the invention. In *re* Sichert, 566 F.2d 1154, 196 USPQ 209 (CCPA 1977). However cast, the underlying finding by the court in these cases was that, based on the factual record of the case, it was clear that the invention could not and did not work as the inventor claimed it did. Indeed, the use of many labels to describe a single problem (e.g., a false assertion regarding utility) has led to some of the confusion that exists today with regard to a rejection based on the “utility” requirement. Examples of such cases include: an invention asserted to change the taste of food using a magnetic field (*Fregeau v. Mossinghoff*, 776 F.2d 1034, 227 USPQ 848 (Fed. Cir. 1985)), a perpetual motion machine (*Newman v. Quigg*, 877 F.2d 1575, 11 USPQ2d 1340 (Fed. Cir. 1989)), a flying machine operating on “flapping or flutter function” (*In re Houghton*, 433 F.2d 820, 167 USPQ 687 (CCPA 1970)), a “cold fusion” process for producing energy (*In re Swartz*, 232 F.3d 862, 56 USPQ2d 1703, (Fed. Cir. 2000)), a method for increasing the energy output of fossil fuels upon combustion through exposure to a magnetic field (*In re Ruskin*, 354 F.2d 395, 148 USPQ 221 (CCPA 1966)), uncharacterized compositions for curing a wide array of cancers (*In re Citron*, 325 F.2d 248, 139 USPQ 516 (CCPA 1963)), a method of controlling the aging process (*In re Eltgroth*, 419 F.2d 918, 164 USPQ 221 (CCPA 1970)), and a method of restoring hair growth (*In re Ferens*, 417 F.2d 1072, 163 USPQ 609 (CCPA 1969)).

Thus catalytic hybridization composition and method comprising multiplex structure involving Watson-Crick base pairing is in the class as Cold Fusion, speculative with out any

structural showing. Therefore the composition comprising multiplex structure and the method involving said structure formation, as claimed in the instant application lacks utility.

#### **Response to Declaration**

Declaration provided by the applicants does not commensurate in scope with claims. It shows an analogous structure but does not provide any basis for Watson-Crick base pairing with more than two strands of nucleic acid.

No claims are allowable.

#### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 703-305-1004. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-0294 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

  
Suryaprabha Chunduru  
June 3, 2002

  
JEFFREY FREDMAN  
PRIMARY EXAMINER